ON THE INTER-RELATIONSHIP OF CALCIUM AND MAGNESIUM EXCRETION. By JOHN MALCOLM.

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THE following is an account of some experiments undertaken with a view to determine whether any relationship exists between the excretion of Ca and Mg such as Bunge has described in the case of sodium and potassium.

By evidence drawn from various sources, Bunge[1] proved that when the ingestion of potassium salts exceeds that of sodium to a certain degree, there results a loss of the latter, and on this ground he explains the desire of herbivora for salt and the popular use of salted food along with potassium-rich vegetables such as potatoes.

Now Calcium and Magnesium are elements which closely correspond in some points to K and Na; they occupy as prominent a place in the intestinal excretion as K and Na do in the urine; further, while all four elements are constantly found in the fluids which bathe living protoplasm[2], the ratio of potassium to sodium is roughly comparable to that of calcium to magnesium.

The first method of investigation adopted was that of a general metabolism experiment in which the total intake and output of Ca and Mg were determined during the following periods. First, a normal period, preceded by a week on the same diet; in the second period the calcium intake was increased and the effect on the magnesium output specially observed; the third was a normal period, and in the fourth, the magnesium intake was increased and the effect on the calcium output noted.

The magnesium and calcium intakes were increased by means of measured quantities of solutions of their chlorides added to the water used in cooking the food.

Two experiments were done in this way on two male dogs. They were confined in special kennels with access only to a large rectangular sloping tray for collection of excreta. The urine was drawn off by catheter thrice daily, and each morning the dogs were taken outside to a paved court for exercise and defæcation. The food consisted of dog biscuit meal and finely ground dried horse-flesh. It was cooked by pouring a measured amount of boiling water over it, and each day's ration was given in two portions.

The urine of every two successive days was evaporated to small bulk on a water-bath, incinerated as a whole in a large porcelain crucible, and the calcium and magnesium estimated in the usual way, the former being precipitated as the oxalate, incinerated and weighed as CaO, while the latter was estimated by weighing as $Mg_2P_2O_7$.

The advantage of using such a large amount of urine was that the final amount of CaO weighed was much greater than would have been obtained by using Neubauer's method.

Disadvantages arose, however, from the fact that no control analyses were possible, and also that, owing to the large amount of phosphate present, some calcium phosphate occasionally came down with the oxalate. For this latter reason the ash was tested for phosphate in each case, and, when it was found to be present, the ash was re-dissolved and the precipitation of the calcium as oxalate repeated.

So far as the total output was concerned such precautions might have been omitted, for, as is well known, the great mass of the calcium output takes place in the fæces, but the urinary calcium was also considered important in this case as showing whether the amount of calcium in the circulating blood was increased. It was not thought necessary to use charcoal or other means to distinguish the fæces of the different periods from each other because it is quite probable that calcium and magnesium may be absorbed from the upper part of the alimentary tract and excreted soon afterwards by the lower parts in advance of the "limiting" agency. The fæces were dried to constant weight; powdered and analysed in 5 grm. portions, after removal of the iron as phosphate.

Results. Tables I, II, III, and IV give the details of the results and the balance in each period.

Magnesium. The Mg output practically balances the intake in both the dogs under the two conditions of experiment. The administration of $CaCl_2$ (in Period II) led to no increased output of Mg, and the increased intake of Mg (Period IV) was accompanied by an almost equally increased excretion. In this last period it may be noted that the increased excretion was distributed in urine and fæces in the same proportion as in the other periods when less Mg was given. Doubling of the Mg intake led to doubling of the urinary as well as of the intestinal magnesium. The ratio of the Mg in the urine to that of the fæces differs in the two dogs, although both were fed on the same meal and flesh. Thus in Dog I the Mg in the urine stands to that of the fæces as 1 : 3 while in Dog II the ratio is 1 to 4·5.

TABLE I. *Magnesium intake and output in Dog I.*

PERIOD I. (normal).

Urine No.	Urine Time	Urine Mg (grms)	Fæces No.	Fæces Time	Fæces Amount (dry)	Fæces % Mg	Total Mg
I.	2 days	?					
II.	2 ,,	·0764	I.	6 days	31·9	0·67	0·2134
III.	2 ,,	?	II.		49·8	0·78	0·3896
Average per day		·038					0·100

Intake = 0·150, output = 0·138 = + ·012 (balance).

PERIOD II. ($CaCl_2$ given).

Urine No.	Urine Time	Urine Mg (grms)	Fæces No.	Fæces Time	Fæces Amount (dry)	Fæces % Mg	Total Mg
IV.	2 days	·1064					
V.	2 ,,	·0970	III.	5 days	22·4	0·72	0·1625
VI.	1 day	·0401	IV.		47·5	0·69	0·3294
Average per day		·048					0·098

Intake = 0·150, output = 0·146 = + ·004 (balance).

PERIOD III. (normal).

Urine No.	Urine Time	Urine Mg (grms)	Fæces No.	Fæces Time	Fæces Amount (dry)	Fæces % Mg	Total Mg
VII.	2 days	·070	V.	2 days	27·9	0·68	0·1918
Average per day		·035					·096

Intake = 0·150, output = 0·131 = + ·019 (balance).

PERIOD IV. ($MgCl_2$ given).

Urine No.	Urine Time	Urine Mg (grms)	Fæces No.	Fæces Time	Fæces Amount (dry)	Fæces % Mg	Total Mg
VIII.	2 days	·1494	VI.	4 days	15·3	1·46	0·1781
IX.	2 ,,	lost	VII.		31·5	1·68	0·5306
			VIII.		15·0	1·17	0·1762
Average per day		·075					0·221

Intake = 0·319, output = 0·296 = + ·023 (balance).

TABLE II. *Magnesium intake and output in Dog II.*

Urine			Fæces				Total Mg
No.	Time	Mg (grms)	No.	Time	Amount (dry)	% Mg	
			PERIOD I. (normal).				
I.	2 days	·0579					
II.	2 ,,	·0613	I.	$5\frac{3}{4}$ days	45·7	0·72	0·3273
III.	2 ,,	·0600	II.		44·2	0·75	0·3330
Average per day		·030					0·115
			Intake = 0·188, output = 0·145 = + ·043 (balance).				
			PERIOD II ($CaCl_2$ given).				
IV.	2 days	·0704					
V.	2 ,,	·0639	III.	5 days	46·1	0·84	0·3962
VI.	1 day	·0342	IV.		45·2	0·86	0·3955
Average per day		·034					0·159
			Intake = 0·188, output = 0·193 = − ·005 (balance).				
			PERIOD III. (normal).				
VII.	2 days	·0678	V.	$2\frac{1}{2}$ days	45·2	0·92	0·4164
Average per day		·034					0·166
			Intake = 0·188, output = 0·200 = − ·012 (balance).				
			PERIOD IV. ($MgCl_2$ given).				
			VI.	$4\frac{1}{2}$ days	32·0	1·59	0·5095
VIII.	2 days	·1313	VII.		30·2	1·82	0·5502
IX.	2 ,,	lost	VIII.		18·5	1·71	0·3169
Average per day		·065					0·306
			Intake = 0·365, output = 0·371 = − ·006 (balance).				

Calcium. The calcium balance is not so perfect in either case as that of Mg. Thus, in Dog I there is a negative balance of ·069 grm., and ·064 grm. in the two normal periods, I and III, = 17 % excess output. In Period II, when the calcium intake was raised by 50 % (·394 grm. to ·588 grm.) the balance was more perfect, nearly 3 % being retained. The chief interest, however, centres in the last period, IV, when the Mg intake was doubled, with the result that the Ca output rose about 33 % (intake ·394, output ·527).

In Dog II, the results are somewhat different. In the normal period, I, there is a + balance of 8 %. In Period II the Ca intake was raised 40 % and the output also rises and exceeds the intake by about 12 %, but for some reason this excess output continues over into the next period. Owing to the long time necessary for drying and analysing the fæces this could not be immediately observed, otherwise this normal period would have been prolonged sufficiently to allow of recovery. In spite, however, of the removal from the system of loosely stored calcium which must have occurred, the administration of $MgCl_2$ in the last period, IV, is accompanied by a marked negative balance (about 22 %). In both experiments the administration of $MgCl_2$ caused a distinct rise in the urinary calcium, and this probably means that the percentage of calcium in the circulating blood had been increased, and that the excess output of Ca was not due simply to the local stimulation of the intestinal tract by the magnesium salt. Such stimulation usually causes a fall of urinary calcium (*e.g.* after castor oil) while opiates have the opposite effect (Rudel [3]).

TABLE III. *Calcium intake and output in Dog I (weight 7·7 kilo.).*

PERIOD I. (normal).

Urine No.	Urine Time	Urine Ca (grms)	Fæces No.	Fæces Time	Fæces Amount (dry)	Fæces % Ca	Total Ca
I.	2 days	·0324					
II.	2 ,,	·0568	I.	6 days	31·9	3·08	0·9841
III.	2 ,,	·0252	II.		49·8	3·37	1·6783
Average per day		·019					0·444

Intake = 0·394, output = 0·463 = − 0·069 (balance).

PERIOD II. ($CaCl_2$ given).

Urine No.	Urine Time	Urine Ca (grms)	Fæces No.	Fæces Time	Fæces Amount (dry)	Fæces % Ca	Total Ca
IV.	2 days	·0316					
V.	2 ,,	·0314	III.	5 days	22·4	4·16	0·9332
VI.	1 day	·0166	IV.		47·5	3·88	1·8427
Average per day		·016					0·555

Intake = 0·588, output = 0·571 = + 0·017 (balance).

PERIOD III. (normal).

Urine No.	Urine Time	Urine Ca (grms)	Fæces No.	Fæces Time	Fæces Amount (dry)	Fæces % Ca	Total Ca
VII.		lost	V.	2 days	27·9	3·17	0·8841
Average per day		(·016)					0·442

Intake = 0·394, output 0·458 = − 0·064 (balance).

PERIOD IV. ($MgCl_2$ given).

Urine No.	Urine Time	Urine Ca (grms)	Fæces No.	Fæces Time	Fæces Amount (dry)	Fæces % Ca	Total Ca
VIII.	2 days	·0527	VI.	4 days	15·3	2·73	·4180
IX.	2 ,,	·1217	VII.		31·5	3·13	·9874
			VIII.		15·0	3·51	·5278
Average per day		·043					·484

Intake = 0·394, output = 0·527 = − 0·133 (balance).

TABLE IV. *Calcium intake and output in Dog II (weight* 9·6 *kilo.).*

Urine			Fæces				
No.	Time	Ca (grms)	No.	Time	Amount (dry)	% Ca	Total Ca
PERIOD I. (normal).							
I.	2 days	·0553					
II.	2 ,,	·0523	I.	$5\frac{3}{4}$ days	45·7	3·31	1·5137
III.	2 ,,	·0560	II.		44·2	3·27	1·4453
Average per day		·027					0·514
Intake = 0·480, output = 0·541 = −0·061 (balance).							
PERIOD II. ($CaCl_2$ given).							
IV.	2 days	·0646					
V.	2 ,,	·0557	III.	5 days	47·1	3·74	1·7633
VI.	1 day	·0543	IV.		46·1	4·08	1·8824
Average per day		·035					0·729
Intake = 0·674, output = 0·764 = −0·090 (balance).							
PERIOD III. (normal).							
VII.	2 days	·047	V.	$2\frac{1}{2}$ days	45·2	3·68	1·664
Average per day		·024					0·665
Intake = 0·480, output = 0·689 = −0·209 (balance).							
PERIOD IV. ($MgCl_2$ given).							
VIII.	2 days	·0782	VI.	$4\frac{1}{2}$ days	32·0	2·88	0·9226
IX.	2 ,,	·0896	VII.		30·2	3·12	0·9421
			VIII.		18·5	3·12	0·5775
Average per day		·042					0·543
Intake = 0·480, output = 0·585 = −0·105 (balance).							

The second mode of investigation used was that of determining to what extent the administration of magnesium can affect the deposition of lime salts in the bones of growing animals[1].

A litter of five young rats was procured and, when eight weeks old, were put into separate cages and fed on dog biscuit meal. Two were used as controls, while the other three were given a small amount of $MgCl_2$ solution in the water used in cooking their food. After six weeks of this treatment they were killed and the total Ca in each estimated.

[1] Recent work by H. Aron (*Pflüger's Archiv*, CVI. p. 91, 1905) shows that potassium salts when given in doses relatively large as compared to the sodium have a deleterious effect on growth of bone.

TABLE V. *Effect of $MgCl_2$ on growing Rats.*

	Controls		$MgCl_2$ given		
	Rat I.	II.	III.	IV.	V.
Weight when experiment began	52	63	59	63	72
Weight when killed	96	106	105	94	143
Total Ca in body	0·8835	1·0290	0·8740	0·8670	1·1140
"Ca expected"	—	—	0·9815	1·0477	1·1956
Difference	—	—	0·1075	0·1807	0·0816
% deficit	—	—	10 %	17 %	7 %

Results (see Table V). At the beginning of the experiment the weights were taken for several successive days at the same hour and then averaged so as to exclude variations due to retained fæces or urine. The control animals weighed 52 and 63 grms., the others 59, 63, and 72 respectively. The total calcium was estimated in the dissolved ash of the whole animal, and the figures given are the result in each case of two estimations in aliquot portions.

The "*Ca expected*" in the rats treated with $MgCl_2$ was calculated from their weights in proportion to that of the control animals at the beginning of the experiment. Thus Rats I and II had a combined weight of 115 grms. and together yielded 1·9125 grms. Ca at the end of the experiment. In the same proportion, Rat III, which weighed 59 grms. to start with, and which received the same food in similar quantity, ought to have yielded 0·9815 grm. Ca, whereas only 0·8740 was found = 10 % less. In Rat IV there was a deficit of 17 % and in Rat V, 7 %.

Another method of examining the results would be to compare the percentages of Ca in the animals at the end of the experiment, but this is less accurate, for the whole body-weight may have been affected by the experimental conditions. These experiments, then, show a distinct diminution in the retention of calcium when the young animal receives a certain amount of soluble magnesium salts in its food.

Although in the literature of calcium metabolism there are no direct references to the subject under consideration, there are some data published by Weiske[(4)] in 1894 which give support to the results of the above experiments. In an investigation on the question of how far other earthy metals may replace calcium in growing bone, Weiske did a series of experiments on a litter of young rabbits, two of which are of importance here. One, Rabbit I, received 1 grm. $CaCO_3$ daily for three months in addition to its food (oats). The other, Rabbit IV, received 1 grm. $MgCO_3$ daily for a similar period, the food being the same.

The rabbits were then killed and the bones were carefully analysed. The weight of dried and fat-free bone in I was 77·45 grms., in IV 69·52, the body-weights of the two being almost equal at the time of death.

The amount of CaO in the skeleton of I = 25·13 grms., in IV it amounted to only 17·62 grms., thus showing a striking diminution. There was a greater amount of organic matter in the bones of IV than of I.

The same diminution is to be observed in two other rabbits of the same series, one of which was given strontium carbonate and the other oats alone.

SUMMARY.

Considerable evidence is brought forward to show that the ingestion of soluble magnesium salts causes a loss of calcium in adult animals and hinders its deposition in young growing animals, while soluble calcium salts do not in the same way affect the excretion of magnesium.

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